strate selective up regulation of atrial IP3R Ca^{2+} release channel mRNA levels. Increased atrial IP3R expression may contribute to the molecular substrate for AF arrhythmogenesis.

11:45

703-6 Vascular Endothelial Growth Factor is Upregulated by Hydrogen Peroxide in Vascular Smooth Muscle Cells and Overexpressed in Atherosclerotic Tissue

J. Ruef, Z.Y. Hu, L.-Y. Yin, F. Li, G.N. Rao, M.S. Runge, C. Patterson. *University of Texas Medical Branch at Galveston, Galveston, TX, USA*

Neovascularization and vascular cell mitosis are hallmarks of neointimal formation in atherosclerotic plaques and restenotic lesions. Vascular endothelial growth factor (VEGF) promotes neovascular growth, whereas oxidative stress is a potent factor in vascular proliferation. To investigate the mechanisms of neovascular formation we treated rat vascular smooth muscle cells (VSMC) with hydrogen peroxide (HP). Northern blot analysis demonstrated a dose-dependent (20 to 500 μM) and time-dependent (0.5 to 6 h) increase in VEGF mRNA with a maximum of 10-fold at 3 h (200 μM HP). As determined by immunoblotting and ELISA, VEGF protein expression and secretion were similarly increased. Human umbilical vein endothelial cells (HUVEC) were treated with conditioned medium from VSMC incubated with 200 μM HP for 4 h. DNA synthesis, measured by thymidine incorporation, was increased by 1.7-fold compared to controls, an effect that was blocked by neutralizing anti-VEGF antibody. The effect of HP on VEGF expression and induction of HUVEC DNA synthesis by conditioned medium could be inhibited by the tyrosine-kinase inhibitor, genestein. HP had no effect on the expression of the VEGF receptor KDR/flk-1 in HUVEC. Immunohistochemical staining of aortic sections from balloon-injured baboons demonstrated increased VEGF expression in the neointima compared to controls. Together, our data suggest that HP is an indirect inducer of endothelial cell growth through release of the angiogenic factor VEGF from VSMC and that oxidative stress is a factor in atherosclerotic neovascularization.

704 Dobutamine Stress Echocardiography

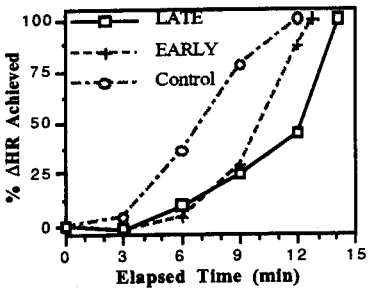
Monday, March 17, 1997, 10:30 a.m.–Noon
Anaheim Marriott, South Hall

10:30

704-1 Reduced Test Time by Early Identification of Patients Requiring Atropine During Dobutamine Stress Echocardiography

T.J. Lewandowski, W.F. Armstrong, D.S. Bach. *University of Michigan, Ann Arbor, MI, USA*

Atropine (AT) is used in patients with inadequate heart rate (HR) response during dobutamine stress echocardiography. The purpose of our study was: 1) to prospectively test an algorithm for early identification of pts requiring AT, and 2) to study the effect of early AT administration on test duration. Two-hundred and nineteen pts were randomized to receive either conventional AT at peak infusion if HR < 100 (LATE) or AT beginning at the end of the second stage (20 μg/kg/min) if HR < 70 (EARLY). AT was required in 86 pts; 35 received AT LATE and 51 were randomized to receive AT EARLY. Of the 51 EARLY pts receiving AT, 82% met criteria for and received AT early, while 18% were missed by the algorithm and received AT at peak. AT dose was 0.80 ± 0.38 mg in EARLY pts and 0.39 ± 0.20 mg in LATE pts. Despite attaining a greater ΔHR, test duration was reduced 1.3 min (9%, p = 0.01). The % of ΔHR achieved vs elapsed time was plotted for both groups and compared to 133 pts who did not receive AT.



In conclusion, pts who require AT during dobutamine echocardiography can be reliably identified before peak stress. Early AT use provided a more balanced physiologic stress and reduced total exposure to dobutamine, thus decreasing test duration and potentially increasing test efficiency.

10:45

704-2 Atropine is not Necessary for Dobutamine Stress Echocardiography

P. Desai, K. Conners, R. Conant, S. Shapiro, L. Ginzton. *Harbor-UCLA Medical Center, Torrance, CA, USA*

Dobutamine (DOB) is used to detect myocardial ischemia. When DOB fails to reach the target heart rate (HR) atropine is often added. *Hypothesis:* atropine will not increase the frequency of ischemia during DOB stress echocardiography (DSE). *Methods:* From January, 1994 to August, 1996, 239 patients (pts) had DSE to diagnose ischemia. DOB was given (5–50) mcg/kg/min. Atropine (0.5–2.0 mg) was added at peak DOB if the HR was <85% of the age-predicted maximal HR. Images were recorded at baseline, at peak DOB and at atropine's peak HR. Wall motion abnormalities (WMA) were scored by 2 echocardiographers blinded to all other data. Ischemia was defined as new or worsening WMA. *Results:* 114/239 pts received atropine. Of these 70 tests were normal, and 44 abnormal. No tests negative with DOB became positive after atropine. Only 4 pts had worse WMA with atropine, changing the result from single-vessel (SVD) to multivessel (MVD) disease.

	Baseline	Peak DOB	Peak Atropine
HR	73 ± 15	113 ± 23*	130 ± 15**
Normal	74	70	70
Ischemic SVD	14	14	10 †
Ischemic MVD	22	30	34 †

* p < 0.001 vs Baseline ** p < 0.001 vs peak DOB † p = NS vs DOB

Conclusions: During DSE adding atropine does not add to the frequency or extent of WMA. Therefore, atropine may not be needed for DSE.

11:00

704-3 Frequency and Etiology of False Negative Results in a Large Unselected Patient Population Undergoing Dobutamine Stress Echocardiography

R. Yeleti, M. Al-Dalli, P. Brenneman, D.S. Segar, H. Feigenbaum, S.G. Sawada. *Krannert Institute of Cardiology, Indiana University, Indianapolis, Ind, USA*

DSE has demonstrated a high sensitivity for the detection of coronary artery disease (CAD) in selected patient populations. To determine the sensitivity and causes of false negative studies in a large unselected population, the results of DSE in 2898 patients were reviewed. *Methods:* Of the 2898 patients who underwent DSE, 565 underwent coronary angiography (CA) within six months of DSE. DSE was considered positive in the presence of a resting wall motion abnormality (WMA) or a stress induced WMA. Significant CAD was defined as a luminal narrowing of >50% in a major epicardial artery. *Results:* The sensitivity of DSE for detecting CAD in all 565 patients was 94% and the specificity was 82%. In the 222 patients without resting WMA, the sensitivity was 83% with 26 false negative exams. The CA of these patients were reviewed to identify potential causes for the false negative tests: 13 patients had lesions with >50% but <70% stenosis; 7 had lesions supplied by collaterals; 4 had disease in distal vessels; and 2 had isolated circumflex artery disease. Nineteen of the 26 had submaximal stress tests. *Conclusions:* In a large unselected patient population, DSE had reasonable sensitivity for the detection of CAD. Patients with false negative exams frequently had submaximal studies with mild to moderate CAD (<70% stenosis, distal disease, or lesions supplied by collaterals).

11:15

704-4 Submaximal Responses to Dobutamine Stress Are Unhelpful in Predicting Subsequent Cardiac Events

R. Ballal, M.-A. Secknus, R. Mehta, M.S. Lauer, T. Marwick. *Cleveland Clinic Foundation, Cleveland, OH, USA*

Exercise tests are considered submaximal (SMX) if pts do not attain target heartrate (ie <85% max age-predicted). The significance of a submaximal (SMX) response during dobutamine echo (DbE) is unclear. Of 1772 pts undergoing standard DbE (Db to peak 40 μg/kg/min with atropine to 1 mg) from 1991–4, 255 pts (14%) had a SMX response and were followed for 2 years.

Results: Pts with SMX were of similar age (62 ± 13 vs 64 ± 12 y) and gender (55% vs 57% men) to the remainder. Resting heart-rate (73 ± 13 vs 75 ± 14) and SBP (144 ± 26 vs 148 ± 27) were comparable. Pts with SMX-DbE demonstrated *ischemia (ISC)* in 46 pts (18%); 20 had coronary

angiograms of whom all had significant coronary disease (CAD). Of 209 pts *without ISC*, 35 had angiograms but only 8 had no CAD. Sensitivity of SMX-DbE was 43% and specificity 100%.

After exclusion of 5 pts lost to follow-up (2%) and 7 pts with revascularization (RVS) within 3 mos of DbE, 243 pts were followed over 2 years. Cardiac death occurred in 20 pts, 45 had infarction or unstable angina and 12 required late RVS. No cardiac events occurred in 166 (68%). While ISC at DbE was predictive of outcome, the event-rate of a negative DbE was greater than in unselected groups;

	ISC+ (n = 42)	ISC– (n = 201)	p
Death (n = 20)	8 (19%)	12 (6%)	0.01
Total events (n = 77)	20 (48%)	27 (28%)	< 0.001

Conclusions: In comparison with reported accuracy and prognostic data in unselected groups, SMX-DbE shows; 1) a low sensitivity for CAD, and 2) less ability to predict favorable outcome. Negative SMX-DbE should be considered non-diagnostic.

11:30

704-5 Intracoronary Dobutamine Echocardiography to Evaluate Multivessel Coronary Artery Disease

J.S. Cohen, A.K. Jacobs, T. Noonan, P. Pearson, R. Davidoff. *Boston Medical Center, Boston, MA, USA*

We have shown that intracoronary (IC) infusion of dobutamine proximal to a stenosis can elicit echocardiographic changes, consistent with ischemia, in patients with single vessel disease (VD). To determine whether this on line functional assessment of individual stenoses is applicable to patients with multivessel disease, we studied 10 stenoses in 7 patients with 2 VD (>70% stenosis). Heart rate (HR), systolic blood pressure (SBP), diastolic pulmonary pressure (PAD) and two dimensional echocardiograms (2DE) were obtained during graded subselective IC infusions of dobutamine (5–100 μg/min) until contractile dysfunction was detected in the region stimulated by dobutamine. Blinded analysis of the 2DE was performed utilizing 16 LV segments and a wall motion score (WMS) ranging from 1 = normal to 4 = dyskinetic. A wall motion index (WMI) was derived as the average WMS for each coronary distribution.

The mean % stenosis was 79.5 ± 3.4. The wall motion in the stimulated territory had a biphasic response with initial improvement and subsequent deterioration at higher doses of dobutamine.

	HR (b/m)	SBP (mmHg)	PAD (mm Hg)	S WMI	NS WMI
Baseline	62 ± 2	132 ± 7	16 ± 1	1.1 ± 0.1	1.1 ± 0.1
Peak	61 ± 4	133 ± 7	14 ± 2	1.8 ± 0.2	1.2 ± 0.1
p value	0.53	0.55	0.07	0.0007	0.26

The stimulated (S) WMI rose from baseline to peak dobutamine dose by 0.70 ± 0.17, consistent with the induction of ischemia. In the non stimulated (NS) territory perfused by the 2nd stenosis, the WMI did not change (p = 0.002 vs S).

Conclusion: In patients with 2VD, IC infusion of dobutamine proximal to a stenosis, does not alter hemodynamics and induces ischemic contractile dysfunction exclusively in the S region supplied by the artery without affecting regions supplied by another significant stenosis. This method holds promise as an on-line assessment of the functional significance of an individual coronary stenosis in patients with multivessel disease undergoing diagnostic catheterization or percutaneous revascularization.

11:45

704-6 Persistent Ischemia Following Dobutamine Stress Echocardiography: An Angiographic Correlation

A.F. Sonel, D. Segar, H. Feigenbaum, R. Kovacs, P. Brennaman, S. Sawada. *Krannert Institute of Cardiology, Indianapolis, Indiana, USA*

The clinical significance of persistent ischemic wall motion abnormalities in the recovery period following dobutamine stress echocardiography (DSE) is unknown. We studied 375 consecutive patients (pts) undergoing DSE (Mean Age 59, 168 males, 207 females). Dobutamine was given up to a maximal dose of 50 μg/kg/min. Echocardiographic images were obtained at rest, low dose (5 or 10 μg/kg/min), peak dose and 6 minutes into recovery. There were 33 pts with ischemia who underwent coronary angiography. Thirteen patients had segments (segs) with transient ischemia (TI) that resolved by 6 min into recovery. Twenty pts had segs with persistent ischemia (PI) that did not resolve by 6 min into recovery. A total of 95 ischemic segs were identified. The location of ischemia was correlated with the angiographic results. Patients with TI had 2.6 ± 0.8 ischemic segs compared to 3.3 ± 1.5 ischemic segs in pts with PI (p > 0.1). Seven percent (4/58) of segs with TI were supplied by totally occluded vessels compared to 35% (13/37) of segs with PI (p < 0.001). Thirty-eight percent (22/58) of segs with TI were supplied by arteries with complex lesions, compared to 70% (26/37) of segs with PI (p < 0.005). Patients with multivessel disease had 22% (13/58) of the segs with TI and 45% (16/37) of the segs with PI (p < 0.025). *Conclusion:* Compared to segments with TI, segments with PI following DSE are more likely to be supplied by vessels with total occlusion or complex lesions and occur more frequently in pts with multivessel coronary artery disease.

705 Three-Dimensional Echocardiography for the Left Ventricle

Monday, March 17, 1997, 10:30 a.m.–Noon
Anaheim Hilton and Towers, Pacific D

10:30

705-1 Three-Dimensional Echocardiography Improves Sensitivity and Specificity of Electrocardiographic Criteria For Detection of Left Ventricular Hypertrophy

A.S. Gopal, D. Roychoudhury, T. Thakur, S. Rao, D.L. King, Z. Shen, M. Lipkowitz, A. Benis, A. Gharavi, R. Phillips. *Mt. Sinai Medical Center, NY, USA*

Background: The sensitivity/specificity of electrocardiographic (ECG) criteria for detection of left ventricular hypertrophy (LVH) have often been determined by 1D echo methods of calculating LV mass that rely on geometric and image position assumptions. Recent data suggest that 3D echo estimates of LV mass which eliminate these assumptions are more accurate and less variable than the 1D method.

Purpose: To compare the sensitivity (SNS), specificity (SPC) of some ECG criteria relative to LV mass by 1D, 2D and 3D Echo.

Methods: 21 hemodialysis patients (6 M, 15 F; 11 African-American, 8 Hispanic, 1 Asian, 1 Caucasian; ages 22–79) underwent 12-lead ECG and 3D Echo (K3 Systems Inc.) with a free-hand scanner (Acuson 128 C/F) using an acoustic spatial locater, line of intersection display, and 8–9 short-axis images. Myocardial mass computed from epicardial and endocardial volumes and indexed to BSA was correlated to several ECG criteria. LVH was defined as >104 g/m^2 in women and >118 g/m^2 in men as established by the anatomic validation of Devereux et al. *Results:*

Criteria	1D Echo		2D Echo		3D Echo	
	SNS	SPC	SNS	SPC	SNS	SPC
Cornell Product	0.60	0.55	0.67	0.63	0.80	0.64
Sokolow-Lyon voltage	0.30	0.73	0.33	0.75	0.40	0.82
Estes Point Score	0.90	0.73	0.75	0.75	0.90	0.82
12-lead voltage	0.40	0.60	0.42	0.75	0.40	0.73
12-lead product	0.20	0.64	0.25	0.63	0.40	0.82

Conclusions: 1) The sensitivity/specificity of ECG criteria improve along with improved accuracy and reliability of echocardiographic measurements of LV mass. Thus, 3D Echo provides the greatest improvement and 2D Echo values are of intermediate sensitivity and specificity between 1D and 3D Echo values 2) An Estes point score of ≥4 had the best sensitivity/specificity in this small African-American/Hispanic hemodialysis patient population.

10:45

705-2 Reproducibility and Day to Day Variabilities of Three-dimensional Echocardiography for Left Ventricular Volumes and Ejection Fraction Calculation With Comparison to Magnetic Resonance Imaging

Y.F.M. Nosir, M.H. Lequin, J.D. Kasprzak, W.B. Vletter, A. Dall'Agata, J. Stoker, R.T. vanDomburg, P.M. Fioretti, J.R.T.C. Roelandt. *Thoraxcenter and Erasmus University, Rotterdam, The Netherlands*

Our aim was to assess the reproducibility and day to day (DD) variabilities of three-dimensional echocardiography (3DE) for calculating left ventricular volumes (LVV) and ejection fraction (EF). Observer variabilities of 3DE were compared with values obtained by magnetic resonance imaging (MRI).

Methods: (A) 15 normal volunteers, and (B) 23 patients with reduced LV function underwent precordial 3DE using rotational acquisition technique (2-degrees intervals with ECG and respiratory gating), and MRI at 0.5 T multislice multiphase ECG-triggered T1 weighted fast field echo. End-diastolic (ED) and end-systolic (ES) LVV and EF were calculated using Simpson's rule